

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SANJAY M. REDDY, BLANCA M. LUPIANI,
and RICHARD L. WITTER

Appeal 2007-2542
Application 10/623,891
Technology Center 1600

Decided: October 26, 2007

Before, ERIC GRIMES, LORA M. GREEN, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the Examiner's final rejection of claims 1-3, 5-10, and 12-15. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The claimed invention relates to vaccines to protect chickens against infection with Marek's disease virus (Specification 1: ¶ 1). "Marek's disease (MD), a highly prevalent and important lymphoproliferative disease of chickens, is controlled in commercial chickens by live virus vaccines consisting of attenuated or naturally avirulent MD-related herpesviruses" (Specification 1: ¶ 2). "Although vaccination programs have been

considered highly effective overall, the poultry industry continues to experience losses due to MD” (Specification 1: ¶ 2). Thus, “there is still a strong incentive to develop even more efficacious products that will protect better in the face of early challenge with very virulent field strains without causing adverse side effects” (Specification 1: ¶ 2).

Claims 1-3, 5-10, and 12-15, which are all the pending claims, stand rejected under 35 U.S.C. § 103(a) as obvious over Witter ’97 (*Avian Diseases*, 41:407-421, 1997), Witter ’95 (*Avian Diseases*, 39: 269-284, 1995), and Jones (*J. Virol.*, 70: 2460-2467, 1996) (Answer 3).

We select claims 1 and 3 as representative of the appealed claims to focus our discussion. Claims 1 and 3 read as follows:

1. A viral agent comprising a recombinant Marek’s disease virus CVI988/X stably transformed with a foreign DNA construct which comprises a long terminal repeat sequence of a reticuloendotheliosis virus, wherein said viral agent is effective to elicit an immune response in a chicken to Marek’s disease virus without causing a significant degree of pathogenicity in said chicken, and further wherein said long terminal repeat sequence is inserted upstream of the ICP4 gene of said Marek’s disease virus.

3. The viral agent of claim 1 wherein said long terminal repeat sequence comprises a Pac I excised DNA segment from Marek’s disease virus strain ATCC PTA-4945.

FINDINGS OF FACT

In concluding that the claimed subject matter would have been obvious over Witter ’97, Witter ’95, and Jones, the Examiner makes the following findings:

1. Witter ’97 describes a recombinant Marek’s disease virus (MDV), designated RM1, which resulted from coculture of virulent MDV strain

JM/102W with reticuloendotheliosis virus (REV) in a duck embryo fibroblast line (Witter '97, at 408, cols. 1-2; Answer 4).

2. RM1 contains a single REV long terminal repeat (LTR) inserted upstream of the MDV IPC4 gene (Jones, at 2466; Answer 10, 15; Appeal Br. 7-8).

3. Witter '97 reports that RM1 was effective to elicit a protective immune response to MDV in chickens, exceeding the response to commercial vaccine strains (Witter '97, at 415-416, 419; Answer 4-5).

4. RM1 also replicated efficiently in vivo (Witter '97, at 416, col. 2) in contrast to the parental strain JM/102W (Witter '97, at 416, col. 1) (Answer 5).

5. RM1 was almost fully attenuated for oncogenicity, "but retained other in vivo properties of virulent viruses such as thymic and bursal atrophy" (Witter '97, at 407 ("Summary"); Answer 5). Thus, Witter '97 concludes that "the RM1 clones would not seem to be likely candidates for commercial vaccine development, primarily because of residual oncogenicity and the ability to cause persistent thymic atrophy" (Witter '97, at 419-420).

6. However, Witter '97 states that RM1 clones "do represent a model for future vaccines" (Witter '97, at 420; Answer 5).

7. Witter '95 reported that MDV vaccine strain CVI988/Rispens does not cause thymic atrophy (Witter '95, at 277 and 274 (Table 5); Answer 5).

8. CVI988/Rispens is described by Witter '95 as generally providing the "best protection" against MDV (Witter '95, at 269 ("Summary"); Answer 5).

THE REJECTION

The Examiner finds that a person of ordinary skill in the art would have been motivated to have utilized the strategy of Witter '97 (Finding of Fact ("FF") 1, 2) to make an attenuated vaccine strain within the scope of claim 1 because Witter '97 describes the advantages of RM1 for vaccine development (immune response; replication; FF 3-4) and suggests it as "a model for future vaccines" (FF 5) (Answer 5-6, 10-11).

The Examiner finds that persons of ordinary skill in would have been motivated to have replaced the MDV strain JM/102W of Witter '97 with the CVI988/Rispens strain of Witter '95 as the target for REV insertion because Witter '95 teaches that CVI988/Rispens does not cause thymic atrophy, a deleterious effect that led Witter '97 to conclude that RM1 would not be a likely vaccine candidate (FF 5; Answer 6; Answer 10-11).

ANALYSIS

In making an obviousness determination over a combination of prior art references, it is important to identify a reason why persons of ordinary skill in the art would have attempted to make the claimed subject matter. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007). The Examiner bears the initial burden, on review of the prior art, of presenting a prima facie case of obviousness. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Here, the Examiner has provided careful reasoning explaining why persons of ordinary skill in the art would have had reason to make the claimed viral agent comprising CVI988/Rispens containing the REV LTR insertion (*see supra* under "The Rejection"). Appellants do not identify a

defect in this reasoning, and as we find none, we conclude that the Examiner has met the burden of providing sufficient evidence to establish prima facie obviousness of claim 1.

Once the Examiner has met his burden, the burden shifts to the applicant to come forward with evidence or argument to rebut the prima facie case. See *Oetiker*, 977 F.2d at 1445, 24 USPQ2d at 1444; *Hyatt v. Dudas*, 492 F.3d 1365, 1369-70, 83 USPQ2d 1373, 1375-76 (Fed. Cir. 2007). Thus, we turn to Appellants' arguments.

Appellants assert that the claimed CVI988 strain transformed with REV LTR replicates faster than the parental strain as a result of the LTR insertion upstream of the ICP4 gene (Appeal Br. 8). They contend that the effect of the insertion to cause increased replication is not disclosed or suggested in the prior art (Appeal Br. 8).

We do not find this argument persuasive. Claim 1 is not limited to a recombinant MDV agent which shows increased replication over the parental strain from which it was derived. Replication rate is not found in claim 1. Thus, Appellants are attempting to distinguish claim 1 from the prior art by a feature which is *not* recited in the claim.

Moreover, "CVI988/X" as recited in claim 1 is directed to a genus of CVI988 strains.¹ It is not evident that enhanced replication of one particular recombinant MDV agent derived from one CVI988 strain would be

¹ "The recombinant Marek's disease virus of this invention is produced by transformation of Marek's disease virus serotype 1 strain CVI988 or any of its clones or serially passaged strains, which are collectively referred to herein as strains CVI988/X. Thus, as used herein CVI988/X includes but is not limited to the previously described original low-passage strain, CVI988/Rispens . . . strain CVI988 clone C (CVI988/C) . . . and CVI988/C/R6" (Specification 13: ¶ 54).

characteristic of all the recombinant agents that are covered by the claim. Thus, even were enhanced replication a property of a particular species within the scope of claim 1, Appellants have not provided evidence that all recombinant MDV agents in the scope of claim 1 would possess this property.

Appellants assert that Witter '97 recognized that the RM1 mutant conferred a high level of protection against MDV, but "admitted that the reason or mechanism for the increase in protection was unknown" (Appeal Br. 9). Thus, Appellants argue that there would have been no reasonable expectation of success that LTR insertion would lead to vaccine efficacy in other MDV strains (Appeal Br. 9).

Witter '97 acknowledges that it "cannot be definitively established" from their results that the properties of RM1 resulted from the insertion of the REV LTR into the unique upstream position in RM1's MDV genome (Witter '97, at 418). However, Witter '97 states that "this possibility is supported" by experimental evidence about how the insertion affected RM1 transcription (Witter' 97, at 418). Thus, while it is not certain that LTR insertion was responsible for the improved the properties of RM1, Witter '97 clearly recognized from their experimental findings that it was probable. Consequently, persons of skill in the art would have reasonably expected that other MDV strains would similarly benefit from insertion of the REV LTR at the same site as in RM1. For obviousness under § 103, all that is required is a reasonable expectation of success, not absolute predictability of success. *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Moreover, by describing RM1 as a "model for future vaccines"

(FF 6), persons of skill in the art would have had reason to have applied Witter '97's teaching about RM1 to other MDV strains.

Appellants also argue that if the process of Witter '97 were repeated, there would have been no reasonable expectation of success that the LTRs would be inserted at the claimed position (Appeal Br. 10). Specifically, Appellants assert that Jones "provides no guidance how the site of insertion could be controlled to ensure insertion of an LTR" upstream from IPC4 (Appeal Br. 11).

We are not persuaded by Appellants' argument. Witter '97 states that cocultivation of MDV and REV results in efficient integration of REV sequences into MDV (Witter '97, at 408). Witter '97 also states that the insertion sites "are not random" (*id.*) and that "inserted retroviral sequences vary but commonly consist of solitary or partial" LTR sequences (*id.*). See also Answer 16. Therefore, it would have been reasonably expected that repeating Witter '97's process with other MDV strains would result in LTR insertion at the same site as in RM1. Jones teaches how to determine the presence and location of an LTR insertion in MDV (*see* Jones, at 2461-2463). Accordingly, we find that it would have been within the level of ordinary skill in the art to determine the presence and location of the LTR in a recombinant MDV viral agent produced by Witter '97's method.

Appellants introduce post-filing evidence that others have "attempted to do just what the Examiner has suggested: to insert the LTRs into the genome of Marek's disease strain CVI-988 at the same location" as the RM1 strain (Appeal Br. 12). "However, despite their efforts, the authors reported that the resultant transformants containing the inserted LTRs did not exhibit enhanced replication. This failure clearly demonstrates that there would be

no predictability or reasonable expectation of success in repeating the process of Witter '97 as suggested by the Examiner" (Appeal Br. 12).

We have considered this evidence, but do not find it persuasive. As noted by the Examiner (Answer 12), claim 1 does not require the recombinant MDV to show "enhanced replication." Thus, Appellants are distinguishing the prior art by a feature which is not present in claim 1. There is also no evidence that all agents within the scope of claim 1 would possess such property. In sum, we do not find Appellants' post-filing evidence persuasive because the feature which Appellants allege to be unpredictable is not found in claim 1.

For the foregoing reasons, we affirm the rejection of claim 1. Claims 2, 5-9, and 12-15, fall with claim 1 because they were not separately argued. *See* 37 C.F.R. 41.37(c)(1)(vii).

Claims 3 and 10

Claim 1 is directed to a viral agent comprising a recombinant MDV which contains an LTR of REV. Claim 3, which is dependent on claim 1, specifies the origin of the LTR as being a Pac I fragment of ATCC PTA-4945.

Appellants assert that the even "if the prior art did suggest inserting an LTR from a reticuloendotheliosis virus into a Marek's Disease virus as proposed by the Examiner (a point which is not conceded by appellants for the reasons noted), the prior art certainly provides no teaching whatsoever how that should be done" (Appeal Br. 14).

We do not find this argument persuasive. "The obviousness analysis cannot be confined by a formalistic conception of the words teaching,

suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents.” *KSR*, 127 S. Ct. at 1741, 82 USPQ2d at 1396. “[W]hen a patent ‘simply arranges old elements with each performing the same function it had been known to perform’ and yields no more than one would expect from such an arrangement, the combination is obvious.” *Id.* at 1740, 82 USPQ2d at 1395-96 (quoting *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 543 (1976)).

In this case, the REV LTR present in the claimed Pac I fragment was known prior to the application filing date (Specification 20: ¶ 69). Appellants use it for the same function as the REV LTR described in Witter ’97. There is no evidence of record that the LTR provided by the Pac I fragment behaves any differently than the LTR of Witter ’97. Accordingly, we find that the use of the Pac I fragment is no more than the conventional use of a known prior art LTR for its expected function as taught by Witter ’97. *See KSR*, 117 S. Ct at 1740, 82 USPQ2d at 1396 (“[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious, . . . a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.”). For the foregoing reason, we affirm the rejection of claim 3. Claim 10 falls with claim 3 because separate reasons for its patentability were not provided. *See* 37 C.F.R. 41.37(c)(1)(vii).

Appeal 2007-2542
Application 10/623,891

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED

LP

USDA-ARS-OFFICE OF TECHNOLOGY TRANSFER
NATIONAL CTR FOR AGRICULTURAL UTILIZATION RESEARCH
1815 N. UNIVERSITY STREET
PEORIA IL 61604